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PATENT SPECIFICATION

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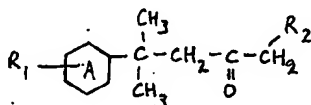
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COMPLETE SPECIFICATION

Aryl and Cyclohexyl Alkanones

We, INTERNATIONAL FLAVORS & FRAGRANCES I.F.F. (NEDERLAND) N.V., a limited liability company organised under Netherlands Laws, of 126, Provincialeweg, Zaandam, Netherlands, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following Statement:—

We have discovered that alkanones of the general structure I

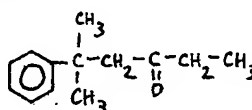


I

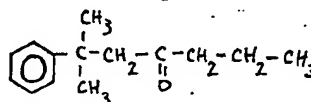
in which R_1 denotes a hydrogen atom or a methyl radical, R_2 denotes a methyl or ethyl radical, and in which A denotes a phenyl or cyclohexyl radical, are characteristic fragrant materials with an outstanding performance in perfume compositions of which they are part, for example perfumes, creams, lotions, powders, soaps, detergents and aerosols.

We have also discovered that compounds according to this invention are excellent flavour and odorant materials.

The following compounds III—IV, which exemplify the above general structure I, have a tenacious and valuable odour which behaves exceptionally well in a variety of perfume and flavour compositions.

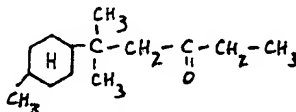


II



III

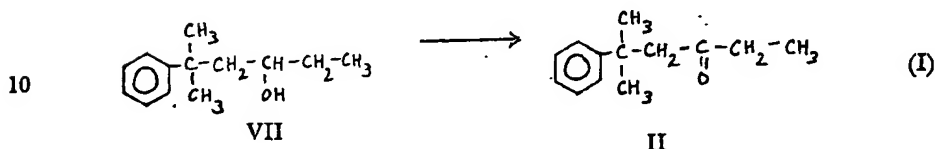
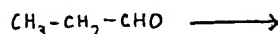
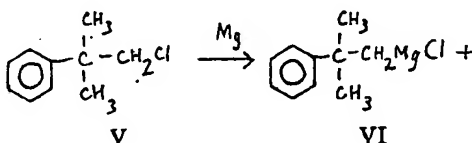
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IV

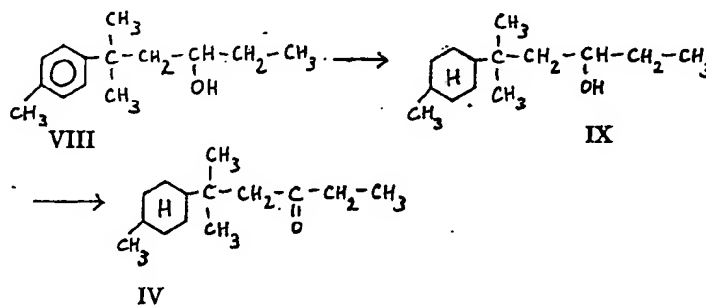
The compounds of the general structural type I can be prepared by several different methods of which the following are mentioned as examples.

5 1st. A general method for the preparation of the alkanones with an aromatic ring (I; A is a phenyl group) is the Grignard reaction of 2-methyl-2-arylpropyl magnesium chloride VI with a lower aliphatic aldehyde, followed by oxidation for example:

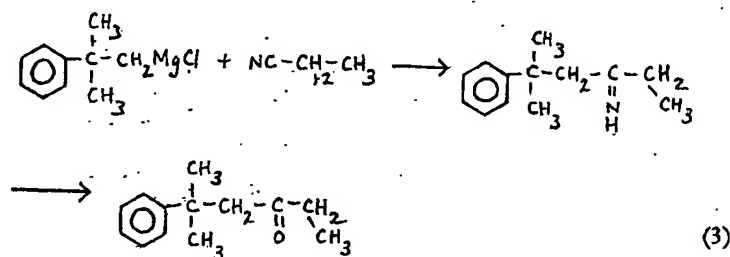


The corresponding chloride V can easily be obtained by condensation of an aromatic hydrocarbon with methallyl chloride according to methods known in the literature. The oxidation can be performed by various classical routes for example with CrO_3 , according to the method of Oppenauer.

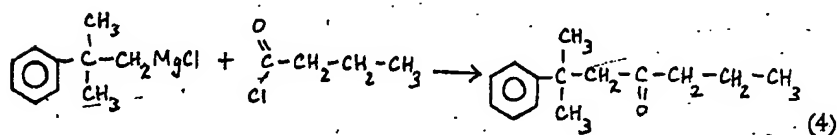
15 2nd. A variant of the method discussed under I can be used for the preparation of alkanones with a 4-methyl cyclohexyl ring. In this case the aryl group of the intermediate alcohol is reduced to the corresponding 4-methyl cyclohexyl group by catalytic hydrogenation, followed by oxidation according to reaction scheme (1) for example



20 3rd. Another variant of the method discussed under I, which yields the aromatic ketones directly, is the Grignard reaction with aliphatic esters containing a hydrocarbon group having up to 5 carbon atoms, or with nitriles or acid chlorides, in the latter case preferably in the presence of cadmium chloride; for example

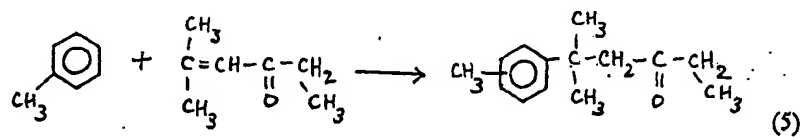


II



III

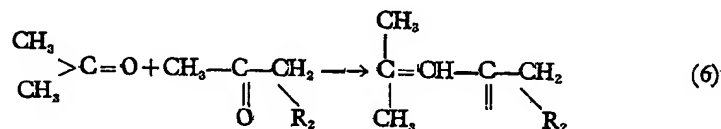
4th. Another general method for the preparation of arylalkanones according to this invention, is the alkylation of an aromatic hydrocarbon with an α,β -unsaturated ketone of the type, e.g.



X

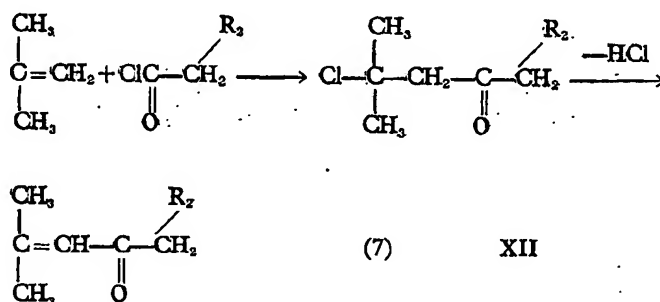
II

The ketone X can be obtained by aldol condensation of acetone with methyl ketones of type XI according to



10 in which R_2 is a methyl or ethyl group.

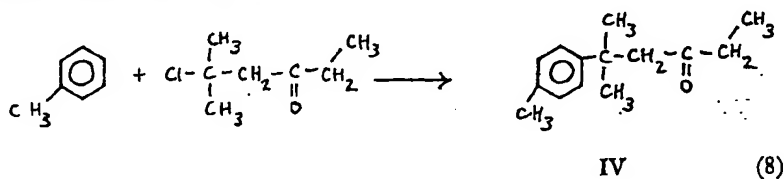
Another method for the preparation of ketones of the type X is found in the Kondakov acylation of 2-methyl propene, for example



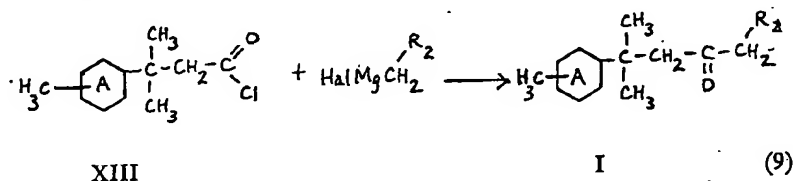
15 in which R_2 is a methyl or ethyl group.

15

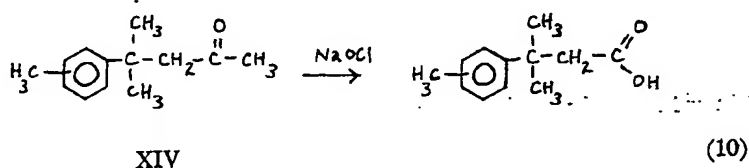
A variant of reaction scheme (5) is the alkylation of an aromatic hydrocarbon with the chloroketone XII, obtained as an intermediate in the preparation of the unsaturated ketones of type X, for example



5th. Another general method for the preparation of alkanones of the structure I is the Grignard reaction scheme (9)

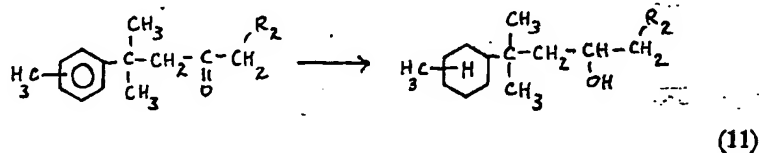


preferably in the presence of cadmium chloride according to a well-known method described in the literature, e.g. D. A. Shirley: Organic Reactions VIII page 31 (1954). The acid chlorides XIII are easily obtainable via oxidation of the methyl ketones XIV with sodium hypochlorite:



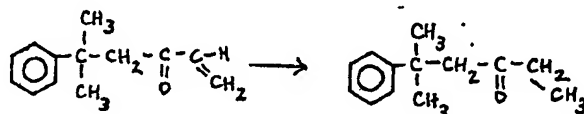
The acids thus obtained can be converted directly into the corresponding acid chlorides XIII (A is a phenyl group) or after catalytic hydrogenation of the aromatic ring.

6th. A general and convenient method for the preparation of alkanones according to this invention, with a saturated ring (I; A is a cyclohexyl group) consists of the catalytic hydrogenation of the corresponding aromatic alkanones into the corresponding cyclohexyl alkanols



followed by oxidation to the ketone as described in reaction scheme (2) par. 2 and according to the methods mentioned under 1.

7th. A general and convenient method for the preparation of alkanones with an aromatic ring (I; A is a phenyl group) is the selective reduction by catalytic hydrogenation of the olefinic double bond of the corresponding arylalkanones disclosed in the specification No. 941,143, for example

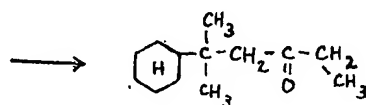


II

(12)

This hydrogenation can be carried out with the common type hydrogenation catalysts such as Raney Nickel at ambient temperature.

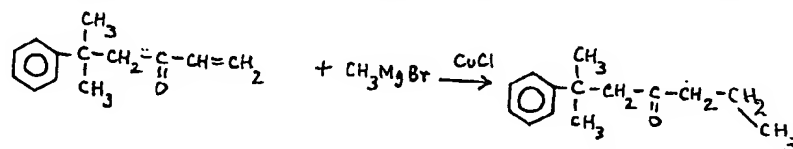
8th. A variant of the hydrogenation method mentioned under method 7 is the complete hydrogenation of the above mentioned arylalkenones to a cyclohexyl-alkanol followed by oxidation to the corresponding ketone (I; A is a cyclohexyl group) as described in methods 1, 2 and 6; for example



(13)

Also in this case the hydrogenation is a general reaction which can be carried out with the common type hydrogenation catalysts at elevated temperatures.

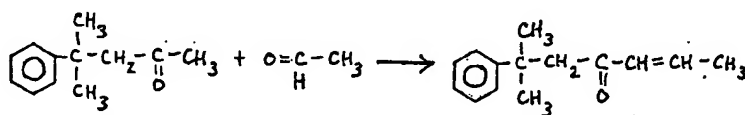
9th. A method which can be used for the preparation of compound III of this invention is the conjugate addition of a Grignard reagent in the presence of cuprous or cupric halides to the arylalkenones cited in methods 7 and 8, for example



III

(14)

10th. A method which can be used for the preparation of a limited number of the compounds of this invention is the aldol condensation of lower aliphatic aldehydes with the methyl ketones XIV mentioned in method 5, followed by hydrogenation of the resulting aryl alkenones, for example

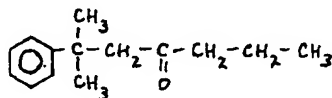


XIV

XV

(15)

Ketone XV can be converted by the hydrogenation procedures described in methods 7 and 8 into



III

The following examples illustrate the preparation of compounds II—IV.

EXAMPLE 1

2-Methyl-2-phenylheptanone-4 (III)

(a) 2-Methyl-2-phenylheptanol-4

To a solution of 2-methyl-2-phenylpropyl magnesium chloride, prepared from 176.5 g (7.26 g atoms) of magnesium 5
1112 g (6.6 moles) of 1-chloro-2-methyl-2-phenylpropane
in 2000 ml of ethyl n-butyl ether
was added with stirring in the course of 2½ hours a solution of 10
432 g (6.0 moles) of n-butanal
in 500 ml of ethyl n-butyl ether.
During the addition the temperature was maintained at 10° to 15°C by cooling with an ice-salt mixture.
After an additional stirring period of 1 hour at 10° to 15°C the reaction product 15
was poured onto a mixture of
3000 g ice
and 500 g (8.3 moles) acetic acid.
The organic layer was separated, washed with water to neutral reaction and the solvent was distilled off. The residue was fractionated through a Vigreux column of 20
30 cm at 2.5 mm Hg pressure which yielded 1096.5 g of the titled alcohol with
b.p. 120° at 2.5 mm; n_D^{20} : 1.5050—1.5061. The yield is 88.7% of theory calculated on butanal.

(b) 2-Methyl-2-phenylheptanone-4

To a mixture of 25
882 g (4.5 moles) of 2-methyl-2-phenylheptanol-4
563 g (1.89 moles) of $\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$
and 450 ml of benzene.
was added in the course of ¾ hour at a temperature of 50° to 55°C, a mixture of 30
900 g (8.82 moles) of H_2SO_4 96%
and 900 g of water.
The reaction mixture was stirred for an additional 2½ hours at 50° to 55°C. Hereafter the organic upper layer was separated and washed with water to neutral reaction. The solvent was distilled off and the residue was flash distilled, yielding 35
853 g distillate, b.p. 90° to 170°C at 3 mm Hg
and 3 g residue.
The distillate was fractionated through a 17-plate Vigreux column giving 810.5 g of 2-methyl-2-phenylheptanone-4, i.e. a yield of 92.7% of the theory, with b.p. 108°C at 3 mm Hg and n_D^{20} : 1.5009.
Gas chromatography demonstrated that the product was pure.

EXAMPLE 2

2-Methyl-2-phenylhexanone-4 (II)

2-methyl-2-phenylhexanol-4 was obtained as follows:

To a solution of 2-methyl-2-phenylpropyl magnesium chloride, prepared from 45
1685 g (10.0 moles) of 1-chloro-2-methyl-2-phenylpropane
267.5 g (11.0 moles) of magnesium
in 3.5 l of dry ethyl n-butyl ether
was added, with vigorous stirring, in the course of 1 hour a solution of
638 g (11.0 moles) of propanal
in 500 ml of dry ethyl n-butyl ether.
During the addition the temperature was maintained at 10° to 15°C by cooling 50
with an ice-salt mixture.
After additional stirring periods of 1 hour at 15° to 20°C and 2 hours at 20° to 25°C the reaction mixture was poured out on a mixture of
4000 g of ice
and 1230 g of concentrated hydrochloric acid. 55
The organic layer was separated and worked up as described in Example 1 under (a), yielding 1513 g of the alcohol, i.e. 78.8% of the theory calculated on the starting chloride, with b.p. 106°C at 3 mm Hg and n_D^{20} : 1.5119.
The 2-methyl-2-phenylhexanol-4 obtained was oxidised with sodium dichromate and sulphuric acid according to the procedure described under Example 1 (b), to yield 60
the ketone in a yield of 84% of the theory, with b.p. 87°C at 1 mm Hg n_D^{20} : 1.5055.

EXAMPLE 3

2-Methyl-2-(4-methylcyclohexyl)-hexanone-4 (IV)

(a) 2-Methyl-2-(4-methylphenyl)-hexanol-4

was prepared from

9125 g (5.0 moles) of 1-chloro-2-methyl-2-(4-methylphenyl)-propane,

132 g (5.43 moles) of magnesium

and 319 g (5.5 moles) of propanal

in the way described in Example 2.

There were obtained 770 g of 2-methyl-2-(4-methylphenyl)-hexanol-4 with b.p. 122°C at 3.5 mm Hg, n_D^{20} : 1.5101. The yield is 74.8% of the theory.

(b) 2-Methyl-2-(4-methylcyclohexyl)-hexanol-4

474 g (2.3 moles) of the alcohol described under (a) were hydrogenated as follows:

A rocking-type autoclave was charged with

474 g (2.3 moles) of 2-methyl-2-(4-methylphenyl)-hexanol-4

265 ml of diisobutyl carbinol

and 20.5 g of Raney Nickel.

Hydrogen was added to a pressure of 2000 p.s.i. and the hydrogenation was carried out at 185°C until the theoretical amount of hydrogen had been absorbed.

The crude reaction product was filtered, the solvent was distilled off at reduced pressure and the residue was fractionated through a 20 cm column packed with Berl saddles at 3 mm Hg pressure. The yield of 2-methyl-2-(4-methylcyclohexyl)-hexanol-4 with b.p. 115°C at 3.5 mm Hg and n_D^{20} : 1.4752 was 418 g, i.e. 85.7% of the theory.

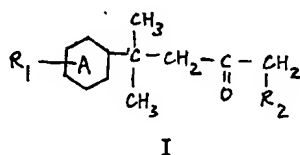
(c) 2-Methyl-2-(4-methylcyclohexyl)-hexanone-4

was obtained as follows from the alcohol described under (b) in a yield of 92.2% of the theory.

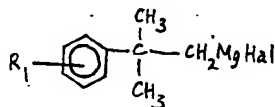
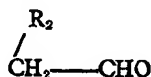
The alcohol described under (b) was mixed with an aqueous solution of $\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$ and oxidised by a mixture of equal parts by weight of 98% H_2SO_4 and water, in the course of 2½ hours at 70°C with vigorous stirring.The reaction mixture was cooled to room temperature and the ketone was extracted from the mixture with toluene. After washing the toluene extract with water to neutral reaction the toluene was distilled off and the residue was flash distilled. The distillate was fractionated through a 20 cm column packed with Berl saddles. B.p. 106°C at 3 mm Hg, n_D^{20} : 1.4660.

WHAT WE CLAIM IS:—

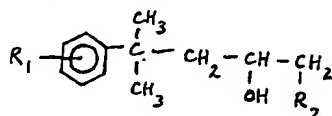
1. Perfume, odorant or flavour compositions containing alkanones of the general structure I

in which R_1 denotes a hydrogen atom or a methyl radical, R_2 denotes a methyl or ethyl radical and in which A denotes a phenyl or cyclohexyl group.

2. A process for the preparation of the compounds I in which A denotes a phenyl or cyclohexyl group, wherein a 2-methyl-2-arylpropyl magnesium halide

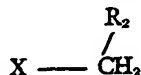
in which R_1 has the meaning specified in claim 1 and Hal stands for a halogen atom, is condensed with an aliphatic aldehyde

in which R_2 has the meaning specified in claim 1, and the alcohol obtained

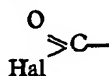


is oxidised to give I, in which A denotes a phenyl group, or prior to said oxidation the aryl group of said alcohol is reduced to the corresponding cyclohexyl group by means of catalytic hydrogenation, in which case the oxidation results in a compound I in which A denotes a cyclohexyl group.

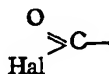
3. A process for preparing a compound I, in which A denotes a phenyl group, wherein the halide defined in claim 3 is subjected to a Grignard-reaction with a compound



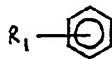
in which X stands for a carbalkoxy group, $\text{NC}-$ or a



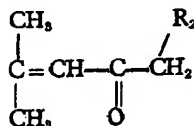
group and R_2 has the meaning specified in claim 1, with subsequent saponification of the imino group if X denotes $\text{NC}-$, and preferably in the presence of cadmium chloride if X denotes



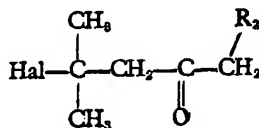
4. A process for preparing compounds I, in which A denotes a phenyl group, wherein an aromatic hydrocarbon



in which R_1 has the meaning specified in claim 1 is condensed with an α,β -unsaturated ketone



or with a haloketone



in which R_2 has the meaning specified in claim 1.

5. A process for preparing compounds I, wherein a Grignard-reaction is effected according to the previously specified reaction scheme (9).

6. A process for preparing compounds I, in which A denotes a cyclohexyl group, wherein a catalytic hydrogenation according to the previously specified reaction scheme (11) is effected with subsequent oxidation of the alcohol obtained to the corresponding ketone.

7. A process for preparing compounds I, in which A denotes a phenyl group, wherein a selective reduction by means of catalytic hydrogenation is effected according to the previously specified reaction scheme (12).

8. A process for preparing compounds I, in which A denotes a cyclohexyl group, wherein the reactions are effected according to the previously specified reaction scheme (13).

9. A process for preparing compounds I, in which A denotes a phenyl group, wherein a conjugated addition is effected according to the previously specified reaction scheme (14).
- 5 10. A process for preparing compounds I, wherein an aldol condensation with subsequent hydrogenation is effected according to the previously specified reaction scheme (15). 5
11. 2-Methyl-2-phenylheptanone-4.
12. 2-Methyl-2-phenylhexanone-4.
13. 2-Methyl-2-(4-methylcyclohexyl)hexanone-4.
- 10 14. The process for the manufacture of alkanones as claimed in claim 1 substantially as described in any of the foregoing Examples 1 to 3. 10
15. Alkanones of the general structure I when prepared as hereinbefore described with reference to the foregoing Examples 1 to 3.

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